Postoperative care of the neurosurgical patient

Martin Siegemund and Luzius A. Steiner

Purpose of review
Monitoring and therapy of patients in neurocritical care are areas of intensive research and the current evidence needs further confirmation.

Recent findings
A consensus statement of the *Neurocritical Care Society* and the *European Society of Intensive Care Medicine* provided pragmatic guidance and recommendations for multimodal monitoring in neurocritical care patients. Only a minority of these recommendations have strong evidence. In addition, recent multicenter randomized controlled trials concerning the therapy of subarachnoidal hemorrhage and traumatic brain injury could not show decreased mortality or improved functional neurologic outcome after the interventions. The current evidence for monitoring and medical therapy in patients after traumatic brain injury and aneurysmal subarachnoid hemorrhage is highlighted in this review.

Summary
Although strong evidence is lacking, multimodal monitoring is of great value in neurocritical care patients and may help to provide patients with the optimal therapy based on the individual pathophysiological changes.

Keywords
elective intradural operation, hyperoxia, multimodal monitoring, subarachnoidal hemorrhage, traumatic brain injury

INTRODUCTION

Neurosurgical critical care patients can be separated in two major groups: neurosurgical emergency cases like traumatic brain injury (TBI) or subarachnoid hemorrhage (SAH) for monitoring the neurological state and early therapeutic interventions, and elective neurosurgical patients for a close-meshed observation of consciousness and neurological deficits to detect hematoma and other early postoperative complications. Particularly regarding the latter group, data are scarce.

Postoperative monitoring of neurosurgical patients undergoing elective surgery

Increased awareness of cost-effectiveness questions the necessity of intensive care admission or early computed tomography (CT) scans [1] for elective neurosurgical patients. A multivariate analysis in a recent retrospective study of 400 elective patients undergoing intradural operations revealed only diabetes and older age to be predictive for postoperative ICU admission [2]. In an accompanying editorial, Hecht *et al.* [3] stated that serious problems after craniotomy mostly occur within the first postoperative hours. They described the transfer of patients to a regular ward after uneventful elective craniotomy after controlling blood pressure and initiating sufficient analgesia. This approach seems feasible, although a lack of correlation in such a small cohort does not mean that these factors alone indicate the need for intensive care [4]. Other relevant factors are intraoperative bleeding, blood product administration, and duration of surgery [2]. To test coagulation sufficiency and the risk of postoperative bleeding, fibrinogen appears to be a modifiable risk factor, as levels below 2 g/l correlate with a 10-fold increase in risk of postoperative hematoma [5]. Together with the fact that delayed ICU admission was not associated with postoperative complications or prolonged length of ICU stay [6], a stepwise approach of ICU or regular ward admission after

Department for Anesthesia, Surgical Intensive Care, Prehospital Emergency Medicine and Pain Therapy, University Hospital Basel Spitalstrasse 21, Basel 4031, Switzerland

Correspondence to Luzius A. Steiner, University Hospital Basel, Basel 4031, Switzerland. Tel: +41 61 265 7254; fax: +41 61 265 7320; e-mail: Luzius.Steiner@usb.ch

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KEY POINTS

- Routine admittance of elective neurosurgical patients after intradural operations should be evaluated in every institution where step-down units can provide a close-meshed surveillance of these patients.
- Although the consensus conference of multimodal monitoring in neurocritical care strongly recommends a wide application of different monitoring techniques, there is still a lack of evidence for many of these techniques.
- There is no evidence for a routine application of magnesium, statins, or progesterone in neurocritical care patients after aSAH or TBI.
- The negative results of the recent large, multicenter, randomized controlled trials should not result in a therapeutic nihilism affecting neurocritical care patients; rather, it should result in an individualized therapeutic approach.

postanesthesia unit care should be considered in further trials.

MONITORING

The *Neurocritical Care Society* and the *European Society of Intensive Care Medicine* have recently published multimodal monitoring guidelines providing pragmatic guidance and recommendations for bedside monitoring of patients receiving neurological critical care [7▪▪]. Alongside the classical monitoring of systemic hemodynamic parameters, intracranial pressure (ICP) and cerebral perfusion pressure (CCP) are the mainstay of neurocritical care monitoring. For guidance of therapeutic interventions, either by parenchymal or intraventricular ICP measurement, the consensus statement provides a strong recommendation supported by high quality evidence [8]. ICP/CPP as a part of multimodal monitoring should be used as the prerequisite for the interpretation of other monitoring devices in protocol-driven care.

In many patients, clinical deterioration occurs before other parameters, such as ICP, alert the clinician [9]. To establish baseline conditions and detect changes in neurological status in most patients, a brief neurological assessment is sufficient. Attention has to be paid to two characteristics: changes in consciousness and focal neurological findings. The latter, for example unilateral paresis, suggests a specific lesion. A deteriorating level of consciousness, however, may signal a variety of conditions, including a rise in ICP, vasospasm after aneurismal subarachnoid hemorrhage (aSAH), or systemic complications. A depressed level of consciousness has been shown to be the most consistent clinical presentation of postoperative intracranial hematoma, with one-third of cases presenting within 12 h of surgery [10]. To facilitate repeated quantitative reporting of the neurological status, standardized scoring systems have been developed. The two most useful scores in neurosurgical patients are the Glasgow Coma Scale (GCS) [11] and the more recently developed Full Outline of UnResponsiveness score (FOUR score) [12]. The GCS, originally developed as a prognostic tool for head-injured patients, is now widely used to estimate the level of consciousness in critically ill patients. There are several shortcomings of the GCS: it may not detect subtle neurological changes, it does not consider brainstem reflexes, and in intubated patients, the verbal response cannot be examined, making the assessment of deeply comatose patients difficult [13]. Although more time-consuming and more difficult to perform than the GCS, the FOUR Score [12] offers important additional information.

Hypoxia and hypotension have been shown to be the two most important systemic secondary insults in patients with TBI [14], and it is reasonable to assume that this also holds true for patients with other forms of brain injury and for postoperative neurosurgical patients. Therefore, oxygen saturation by pulse oximetry and blood pressure are continuously monitored. Although evidence is lacking, continuous intra-arterial blood pressure monitoring is a common practice in neurosurgical patients because even short periods of hypotension may compromise cerebral perfusion and oxygenation. The regional measurement of brain tissue oxygen pressure or jugular bulb oximetry and brain metabolism by means of microdialysis are strongly recommended by the new monitoring guidelines, despite the availability of only low-quality evidence [7▪▪]. Both techniques provide valuable information about integrity and oxygen supply of the local brain microcirculation and can be used to guide medical therapies such as blood transfusion, hyperoxia, or therapeutic hypothermia. Especially the application of high inspiratory oxygen concentrations needs more than the usual monitoring by blood gas analysis and pulse oximetry. After adjustment for different possible confounding factors, both hyperoxia and hypoxia were associated with an increased risk of mortality [15,16] or delayed cerebral ischemia [17]. Despite the clear advantage of an adequate oxygen supply to brain tissue at risk, supranormal oxygen partial pressures seem to harm brain cells through the generation of oxygen and nitrogen free radicals [18] and an increase in cerebral excitotoxicity because of glutamate [19]. In addition to local oxygen metabolism, cerebral microdialysis can be

used to monitor consequences of systemic glucose variations and the concentration of local neurotoxic substances [20].

The arterial partial pressure of CO_2 ($PaCO_2$) is an important determinant of cerebral blood flow (CBF). However, the linear relationship between CBF and $PaCO_2$ may be altered in some neurosurgical patients [21]. Nevertheless, monitoring of $PaCO_2$ is general practice. In particular, patients with low intracranial compliance have a significant risk of developing raised ICP with rising $PaCO_2$. There is some controversy as to the usefulness of end-tidal CO_2 ($ETCO_2$) as an indicator of $PaCO_2$ in neurosurgical patients. Three studies specifically addressed the problem of reliability of $ETCO_2$ in head-injured patients [22–24]. Of these three, one reported a good correlation between the two methods [22], whereas the most recent article reported that the $PaCO_2$ and $ETCO_2$ varied considerably, and that the $PaCO_2$-$ETCO_2$ gradient was not stable over time [24]. As pulmonary problems are frequent in neurosurgical patients, we suggest that $PaCO_2$ rather than $ETCO_2$ be monitored whenever possible.

Subarachnoidal hemorrhage

Compared with patients who underwent endovascular coiling, those who underwent surgical clipping seemed to have a significantly higher probability of death or functional dependency [25]. The unfavorable outcome in the clipping group does not seem to result from vasospasm-induced delayed cerebral ischemia (DCI) and cerebral infarction [26] because the incidence of these complications is similar after clipping or coiling of aneurysms in the anterior circulation [27,28]. Prophylaxis, detection, and therapy of cerebral vasospasms to prevent delayed neurological deficits after SAH are of great importance.

Transcranial Doppler ultrasonography (TCD) remains the most important monitoring method to estimate CBF after repair of aneurysmal bleeding, despite differing accuracy caused by operator variability [29]. High-quality evidence demonstrates that TCD can predict angiographic-confirmed vasospasm [30,31] and with less accuracy the development of delayed ischemic neurological deficits [32].

Beside the key role of TCD in the monitoring of patients with SAH, the role of other monitoring modalities is not so clear. The 2011 *Neurocritical Care Society's Multidisciplinary Consensus Conference* recommended no specific monitoring for cardiac function, intravascular volume status, or other regional neurophysiological monitors in patients following aSAH [33]. In a prospective, multicenter, cohort study, echocardiographic wall motion abnormalities were independent risk factors for poor clinical outcome after SAH [34]. Delayed cerebral ischemia only partially explained this relationship. Cardiac dysfunction was also associated with a poor-grade aSAH and consecutive rapid and sustained catecholamine release [35].

In poor-grade SAH patients, monitoring of ICP over a therapeutic ventricular drainage already in place or an intra-parenchymal probe seems to be valuable because increased ICP is common in these patients early after SAH [36]. A lack of reaction to therapeutic approaches aiming at a lower ICP appeared to be associated with early brain injury, poor clinical outcome, and mortality [36,37].

The incidence of DCI and early brain injury seems clearly related to the intravascular volume status, and the 2011 recommendations proposed euvolemia as a target for intravascular volume management [33]. Because classical triple-H therapy consisting of hypertension, hemodilution, and hypervolemia did not prophylactically or therapeutically prevent cerebral vasospasm and DCI [33,38], new monitoring and volume resuscitation strategies have been tested. In their recent study including 204 SAH patients, Yoneda *et al*. [39] showed that the cardiac index measured by transpulmonary thermodilution was significantly lower in patients with poor-grade aSAH and that patients developing DCI had a significantly lower global end-diastolic volume index (GEDI) than patients without these neurological sequelae. The same study group was able to show that the GEDI was an independent risk factor associated with the occurrence of DCI and severe pulmonary edema [40], the *Scylla and Charybdis* of volume therapy in aSAH. They found a lower threshold of 822 ml/m^2, slightly above the normal range, correlated with an increased risk of DCI. A GEDI threshold above 921 ml/m^2 was best correlated with the occurrence of severe pulmonary edema in 47 of 180 patients after aSAH [40]. The infusion of crystalloid or colloid infusion to increase the cardiac index and raise GEDI above normal values reduced DCI and improved postoperative functional outcome in poor-grade SAH patients [41]. Application of fluid boluses that increased cardiac index in parallel to GEDI was also associated with a significantly higher increase of regional brain tissue oxygen pressure in patients after SAH [42]. In a prospective randomized double-blind trial, the use of isotonic saline for fluid boluses after aSAH was associated with hyperchloremia, hyperosmolality, and a positive fluid balance, whereas patients receiving balanced crystalloid infusion did not show electrolyte disturbances or hypoosmolality [43].

The increase of oxygen transport capacity to improve microvascular oxygenation in brain tissue at risk is also known to prevent DCI in patients after aSAH, although no critical hemoglobin concentration is known [44▪]. In general, a threshold of 7 g/l in ICU patients is standard, as higher values seem to increase mortality. Within the scope of multimodal monitoring, measurement of local brain oxygen partial pressure is a possibility to monitor the effect of red blood transfusion, especially because transfusions may increases venous thromboembolism and thrombotic events [45].

For more than a decade, intensive care support of patients after aneurysmal SAH has consisted of administration of statins and magnesium in addition to prophylactic nimodipine treatment. Recent work challenges this approach. A recent multicenter, randomized, double-blind trial showed that intravenous magnesium sulphate does not improve clinical outcome after SAH. The authors concluded that routine administration could not be recommended [46]. Nevertheless, in a recent meta-analysis, DCI was the only outcome with a statistically significant effect favoring magnesium treatment [47]. This meta-analysis also concluded that prophylactic use of magnesium is not supported by current evidence, as functional outcome was not improved.

Enhancement of CBF, anti-inflammation, and increased endothelial nitric oxide production were potential beneficial effects justifying the use of statins for prevention of cerebral artery vasospasm and consecutive DIC [44▪]. Although 80 mg of simvastatin for 2 weeks decreased the number of patients with high blood velocities in TCD and neurologic deterioration, there was no improvement in functional outcome [48]. In a double-blind randomized controlled trial of 800 patients after SAH, the application of 40 mg of simvastatin for 3 weeks did not improve functional neurological outcome after 6 months [49▪]. The authors also performed a small meta-analysis dominated by their own data, which did not show any benefit of statins on short or long-term outcome in these patients. The authors do not recommend not treating patients with simvastatin after SAH.

Several groups of direct vasodilator drugs have been tested for reduction of angiographic vasospasm and DCI. The endothelin A receptor antagonist clazosentan indeed reduced vasospasm but without a significant effect on functional outcome [44▪,50,51]. Rho-kinase inhibitors like fasudil and eicosapentaenoic acid, which reduce smooth muscle contraction, lower the incidence of angiographic vasospasm and cerebral infarction, and increase the probability of good recovery [44▪,52]. The phosphodiesterase-III inhibitor cilostazol has antithrombotic as well as cardiac and vasodilatory effects. In two recent trials, cilostazol significantly decreased angiographic vasospasm and cerebral infarction and showed an improved clinical outcome [53,54]. Antithrombotic therapy with low-dose intravenous heparin (8–10 U/kg/h), 12 h after securing the aneurysms, reduced the incidence of clinical vasospasm and delayed infarction after SAH without clinically significant hemorrhage [55]. Although applications of antiplatelet drugs also seem to reduce poor outcome, they showed a trend toward increased cranial hemorrhage [44▪]. Antithrombotic therapy warrants further clinical investigation.

Traumatic brain injury

Patients with severe TBI are usually admitted to intensive care for early clinical recognition of neurological deterioration, prevention of secondary cerebral ischemia, and monitoring and therapy of ICP or CCP [56]. Actual guidelines propose an ICP below 20 mmHg as threshold for treatment [57]. A single episode of an ICP above 20 mmHg for more than 15 min is an adequate predictor of poor outcome, whereas a CPP below 50 mmHg for the same time period did not affect survival [58]. Although the value of ICP measurement was recently questioned [59], we believe that ICP monitoring combined with continuous brain tissue oxygen measurement [60,61] provides the best information about regional microcirculatory perfusion in the brain. In contrast to acute ischemic stroke, cerebral perfusion CT cannot be performed regularly in patients with severe head injury. In a very recent study, the combination of ICP monitoring together with brain tissue oxygen pressure and cerebral microdialysis [62] was more accurate in predicting cerebral hypoperfusion measured by perfusion CT scan than ICP measurement alone [60].

To maintain adequate CPP, isotonic saline for fluid resuscitation and norepinephrine are usually used in patients with severe head injury. In case of arrhythmias or refractoriness to norepinephrine, vasopressin seems to be a valuable alternative for blood pressure support [63]. Isotonic saline potentially causes hyperchloremic acidosis and reduced renal blood flow. A recent study showed that balanced crystalloid infusion can be used in TBI patients without any increase in ICP or mortality, and that this type of infusion reduces hyperchloremic acidosis [64].

Increased ICP was traditionally treated with a stepwise approach [56]. After intensification of analgesia and sedation, hyperosmolar therapy, usually

using mannitol, was started. Mannitol decreases ICP first by reducing CBF and after establishing an osmotic gradient by extraction of water from brain tissue [65]. After degradation and elimination of the mannitol molecules, osmotic equilibrium is re-established. In contrast, bolus administration of hypertonic saline was more effective in lowering the cumulative and daily ICP burden after severe TBI and significantly reduced ICU length of stay [66]. Effectiveness of osmotic therapy depends on an intact blood-brain barrier. In a small study, more than one-third of patients treated with hypertonic saline had an impairment of passive blood brain barrier function, a higher ICP, and a trend toward increased mortality [67]. Continuous application of half-molar sodium lactate after TBI for 48 h reduced episodes of increased ICP and reduced fluid and chloride load [68,69]. Sodium lactate may also be used as an alternative energy substrate in conditions of increased energy demand and limited glucose availability [70]. Beside the ICP-lowering effect, sodium lactate decreased brain tissue concentration of the excitotoxic neurotransmitter glutamate and increased the concentration of lactate and pyruvate after TBI [69].

Therapeutic hypothermia is another option to decrease ICP after severe head injury [56]. Until now, no clear evidence exists that hypothermia (at 32–34°C) effectively influences functional neurological outcome by decreasing ICP [71]. Currently, the large multicenter EUROtherm3235 trial has closed recruitment of patients with severe TBI [72]. This trial is investigating influence of early therapeutic hypothermia for 48 h followed by a rewarming phase, (+0.25°C/h) on mortality and functional outcome [73].

If classical intensive care procedures to lower ICP fail, surgical interventions like cerebrospinal fluid drainage and decompressive craniectomy are last resorts. Despite the persuasive concept of enlargement of possible volume for cerebral edema, a large clinical trial could not confirm the presumed benefits of decompressive craniectomy [70,74]. In patients with diffuse head injury, craniectomy within 72 h after trauma had the same mortality as patients receiving intensive medical treatment, but the rate of unfavorable neurological outcome was significantly higher. The 'Randomised Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of Intra-Cranial Pressure' (RESCUEicp) trial has completed recruitment, and data are awaited after follow-up and data analysis has been completed [75].

Different response to TBI between sex as well as the results of small phase II trials and animal experiments has led to increased research on hormone therapy [71]. In animals, progesterone reduced cerebral edema, neuronal loss, and behavioral alterations [70]. Two large multicenter trials investigated the influence of progesterone therapy for 4–6 days on functional outcome and mortality. Although, together, both studies included nearly 2000 patients, no benefit could be found in patients treated with progesterone after TBI [76,77]. Erythropoietin also showed anti-inflammatory, antiapoptotic, and vascular neuroprotective mechanisms in experimental models. Application of 500 IU/kg of erythropoietin and a transfusion threshold of 100 g/l were tested in 200 patients [78]. Neither the administration of erythropoietin nor the maintenance of hemoglobin concentrations above 100 g/l resulted in improved functional outcome after 6 months.

In the recent consensus guidelines on multimodal monitoring, regular wake-up tests and sedation interruption are not recommended for patients at increased risk for intracranial hypertension [13]. In an average population of ventilated intensive care patients, daily interruption of sedation resulted in a higher amount of sedative use and nurse-related workload without decreased ventilation time or ICU length of stay [79]. In patients with TBI or SAH, the daily interruption of sedation has the risk of a prolonged elevation of ICP accompanied by a decrease in CPP [80] and brain tissue oxygen tension [81]. Current guidelines recommend additional monitoring for cerebral ischemia should patients with increased ICP require controlled hyperventilation to decrease CBF [61]. Patients with severe head injury and prolonged mechanical ventilation may benefit from early tracheostomy. In an observational propensity-matched cohort study, tracheostomy before day 9 decreased ventilator time, length of ICU, and hospital stay but not in-hospital mortality [82].

CONCLUSION

Despite the lack of high-grade evidence for most interventions in the care of emergency neurosurgical patients, there is a broad consensus on how to monitor and treat intensive care patients after neurological emergencies. The results of ongoing prospective, randomized, multicenter trials will shed some light on the future therapy of neurointensive care patients [73,75]. Although evidence from the above-mentioned studies is very much appreciated, preliminary research focusing on solid evidence regarding monitoring and therapy is urgently needed.

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Conflicts of interest

There are no conflicts of interest.

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